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10/565,346	01/20/2006	Jane Hirsh	CPX-015.01	1923

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EXAMINER
HAGHIGHATIAN, MINA

ART UNIT	PAPER NUMBER
1616	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/565,346	HIRSH ET AL.	
	Examiner	Art Unit	
	MINA HAGHIGHATIAN	1616	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *01 December 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1 and 3-13* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1 and 3-13* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *11/04/08*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Receipt is acknowledged of the Amendments, Remarks and Terminal Disclaimers filed on 10/10/08 and an IDS filed on 11/04/08. Claim 12 has been amended, and no claims cancelled or added. Accordingly, claims **1 and 3-13** are pending. Receipt is also acknowledged of the request for Pre-appeal Brief review filed on 12/01/08. Applicant's arguments were considered persuasive. Accordingly, prosecution is reopened.

Rejections and/or objections not reiterated from the previous Office Action are hereby withdrawn. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set of rejections and/or objections presently being applied to the instant application.

Note: claims appear to contain certain typographical errors such as the name of active agents (e.g. alclometasone, beclamethasone, etc).

Terminal Disclaimer

The terminal disclaimers filed on 10/10/08 disclaiming the terminal portion of any patent granted on this application which would extend beyond the expiration date of any patent granted on said Applications have been reviewed and are accepted. The terminal disclaimers have been recorded.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 1 and 3-13 are rejected under 35 U.S.C. 103(a) as being unpatentable over Tamarkin et al (US 20060140984) in view of Davis (5,143,717) and in further view of Sachetto (WO 9603115A1).

Tamarkin et al disclose an alcohol-free cosmetic or pharmaceutical foam carrier comprising water, a hydrophobic solvent, a foam adjuvant agent, a surface-active agent and a water gelling agent (see abstract). The said alcohol-free foamable carriers, when placed in an aerosol container and combined with a liquefied gas propellant, create an oil in water emulsion, which upon release from the aerosol container, provides a therapeutically beneficial foam product (see [0025]). The foam carrier includes active agents, both water soluble and oil soluble (see [0063]). The foam is easily spreadable,

allowing treatment of large areas as the arms, back, legs and breast (see [0064]). Examples of suitable propellants include volatile hydrocarbons such as butane and fluorocarbon gases (see [0115]). Examples of suitable active agents include antibiotics, antifungals, anesthetics, anti-inflammatory agents, corticosteroids, etc (see [0226]). Anti-inflammatory agents include clobetasone, betamethasone, diclofenac, ketorolac, ibuprofen (see [0245] and [0252]-[0257]). Antifungals include fluconazole, ketoconazole, clotrimazole, etc (see [0234] to [0237]). Antibiotics include penicillins, macrolides, beta-lactams, etc ([0229]). Anesthetics include lidocaine, bupivacaine, dibucaine, etc (see [0264]). Example 8 discloses a foam formulation comprising antibacterials in an amount of about 2%. Example 9 discloses a foam formulation comprising 1-2% antifungals. Example 10 discloses foam formulations comprising 0.05 to 1% of corticosteroid anti-inflammatory agents. Example 18 discloses a foam formulation comprising 4% lidocaine. Example 1 discloses a method of preparing the foam formulations.

Tamarkin et al lacks disclosure on the oil phase being solid or semi-solid at room temperature. This deficiency has been remedied by Davis. Tamarkin et al also lacks specific disclosure on hydrofluroalkanes as propellants. However this deficiency has been cured by Schetto.

Davis teaches burn foam and delivery system. The said foam is an antibiotic formulation useful in the treatment of burns and abrasions and adapted for topical application as a clinically water soluble foam (see abstract). The process steps in preparation of the said foam formulation include **heating and melting** the white

petrolatum and other ingredients until all dints are melted and thoroughly to form the **oil phase** of the emulsion (see col. 4, lines 26-40).

Sachetto teaches aqueous foamable compositions comprising active agents surfactants and foaming agents. The foaming agent is preferably a so-called liquefied gas, including butane, isobutene or environmentally friendly propellants such as HFA 134a and HFA 227 (see page 4 and Table 1). Such foamable formulations have been exemplified in examples 1-21. Tables such as Table IV, discloses ingredients used in examples 10-14, which include a foaming agent.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to have combined the teachings of Tamarkin et al, Davis and Sachetto on forming foam compositions with a reasonable expectation of successfully preparing stable foam formulations for treating various disorders topically. Tamarkin et al teach an alcohol-free foam composition where the oil phase is liquid at room temperature and Davis teaches a foam formulation where the oil phase is solid at room temperature. Tamarkin discloses that the foam formulations comprise a propellant and Sachetto discloses that propellants such as HFAs are suitable and environmentally friendly propellants and are used in foam formulations. One of ordinary skill in the art could have selected the solid phase of Davis over the liquid phase of Tamarkin et al with predictable results. In other words, **all the claimed elements** were known in the prior art and one skilled in the art could have combined the elements as claimed by

known methods with no change in their respective functions, and the combination would have yielded predictable results to one of ordinary skill in the art at the time of the invention.

Claims 1 and 3-13 are rejected under 35 U.S.C. 103(a) as being unpatentable over Tamarkin et al (US 20060233721) in view of Quigley, Jr. et al (6,075,056) and in further view of Sachetto (WO 9603115A1).

Tamarkin et al teach foamable composition for administration to the skin, body surface, body cavity or mucosal surface, e.g. the mucosa of the nose, mouth, eye, ear, respiratory system, etc. The foamable oil in water emulsion composition includes: an oil globule system, selected from the group consisting of oil bodies; and sub-micron oil globules, about 0.1% to about 5% by weight of an agent, selected from the group consisting of a surface-active agent, having an HLB value between 9 and 16 and a polymeric agent and a liquefied or compressed gas propellant at a concentration of about 3% to about 25% by weight of the total composition, water and optional ingredients are added to complete the total mass of 100% (see abstract and [0012]). The said foamable composition further includes at least one therapeutic agent such as an anti-inflammatory agent, antifungal or antibacterial, anesthetics etc (see [0026]). A polar solvent such as polyols ([0064]). The foamable compositions may be substantially alcohol-free, i.e. **free of short chain alcohols**, having up to 5 carbon atoms in their carbon chain skeleton (see [0066]). The formulations may be in an oil-in-water emulsion

([0080]). Suitable propellants include volatile hydrocarbons and fluorocarbon gases ([0098]). Claim 1 is drawn to a foamable oil in water emulsion composition comprising an oil globule, a non-ionic surface active agent, water and a liquefied propellant.

Tamarkin et al does not disclose an oil phase wherein the emulsion is a solid or semi-solid at room temperature. This deficiency has been remedied by Quigley, Johann R. Richter Supervisory Patent Examiner Technology Center 1600. et al. Tamarkin et al also lacks specific disclosure on hydrofluroalkanes as propellants. However this deficiency has been cured by Schetto.

Quigley, Jr. et al teach stable topical formulations comprising an antifungal agent and an anti-inflammatory steroid useful for treating fungal diseases and their related inflammation (see abstract). The topical formulations may be in the form of foam, cream, lotion, solution, etc (see col. 7, lines 31-34). To prepare the oil phase of the said topical formulations, it is said that the drugs are dissolved in the oil phase consisting of melted oil-soluble components of the formulation prior to addition of this phase to the aqueous phase (see col. 8, line 65 to col. 9, line 3). Other examples disclose similar process steps. Quigley also discloses that “white petrolatum is an emollient cream base and can be replaced by mineral oil” (see col. 8, lines 50-51).

Sachetto teaches aqueous foamable compositions comprising active agents surfactants and foaming agents. The foaming agent is preferably a so-called liquefied gas, including butane, isobutene or environmentally friendly propellants such as HFA

134a and HFA 227 (see page 4 and Table 1). Such foamable formulations have been exemplified in examples 1-21. Tables such as Table IV, discloses ingredients used in examples 10-14, which include a foaming agent.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to have combined the teachings of Tamarkin et al, Quigley, Jr. et al and Sachetto on stable topical formulations comprising active agents such as antifungal agents and anti-inflammatory steroids useful for treating various diseases with a reasonable expectation of successfully preparing stable and effective topical foam preparations. Tamarkin et al teach foam formulations wherein the oil phase is a liquid at room temperature and the formulations are substantially free of lower alcohols. Quigley teaches topical formulations that can be in the form of foam and wherein the oil phase of the oil-in-water emulsion is soli or semi-solid at room temperature and is mixed with the aqueous phase after being melted. Tamarkin discloses that the foam formulations comprise a propellant and Sachetto discloses that propellants such as HFAs are suitable and environmentally friendly propellants and are used in foam formulations. One of ordinary skill in the art would have been able to select the solid oil phase of Quigley and the substantially free of alcohols foam formulation of Tamarkin et al with expected results. That is, **all the claimed elements** were known in the prior art and one skilled in the art could have combined the elements as claimed by known methods with no change in their respective functions, and the combination would have yielded predictable results to one of ordinary skill in the art at the time of the invention.

Additionally, the claims would have been obvious because a person of ordinary skill has good reason to pursue the known options within his or her technical grasp. If this leads to the anticipated success, it is likely the product not of innovation but of ordinary skill and common sense.

Claims 1 and 3, 5-9, 11-13 are rejected under 35 U.S.C. 103(a) as being unpatentable over Beutler et al (4,808,388) in view of Henry (5,858,331).

Beutler et al **Foamable** cosmetic creams for application onto the skin, comprising a selected creamy **oil-in-water emulsion** and a selected propellant, which may be and advantageously is a **single propellant gas**, are disclosed. Improvement of the froth properties is effected by predetermined control of the ingredients of the composition and their proportions, comprising specific percentage ranges of nonionic emulsifier, oil portion, consistency-providing agent, and water, a viscosity of the starting cream emulsion formed therefrom between about 200 and 500 mPas, and the propellant employed, which consists essentially of nitrous oxide or carbon dioxide, preferably nitrous oxide (see abstract).

Beutler et al also discloses that the starting emulsion contains between about 2 and 9 percent by weight of nonionic emulsifying agent, between about 4.5 and 21 percent by weight of oil portion, and between about 0.5 and 4.5 percent by weight of consistency-providing agent, the balance being water to 100 percent by weight, and it must have a viscosity of between about 290 and 500 mPas. The nonionic wetting agent

employed can be, for example, an alkyl polyglycol phosphoric acid ester, glyceryl stearate, PEG glyceryl stearate, PEG stearate, PEG stearyl or PEG cetyl stearyl ether, each by itself or in combination with one another. The oil portion is selected, for example, from fatty substances such as vegetable and mineral oils, liquid fatty alcohols, and liquid waxes. The consistency-providing agent suitably employed may be, for example, selected from macro-molecular gel builders, fats, waxes, and alcohols of long-chain fatty acids (see col. 2, lines 27-50). Working examples 1-9 show various amounts and ingredients suitable for preparing the said foam formulations.

Beutler et al lacks disclosure on the incorporation of the specific active agents and also HFAs being used as propellants. These deficiencies are cured by Henry.

Henry teaches prilocaine base in liquid form which can be solubilized within hydroflurocarbon propellants to produce a stable oily liquid (see abstract). It is disclosed that Chlorofluorocarbon (CFC) propellants have been widely used in aerosol formulations; however, CFC propellants are being phased out under international treaties due to their possible adverse impact on the ozone layer. Hydrofluorocarbon (HFC) propellants have been investigated extensively as substitutes for CFCs. Thus one object here is to provide a method of using prilocaine as a solubilizing agent in HFC propellants (see col. 2, lines 48-67).

Henry teaches that prilocaine in base form has been found to be soluble in the HFC propellants 1,1,1,2-tetrafluoroethane and 1,1,1,2,3,3,3-heptafluoropropane. Prilocaine is soluble when combined with the HFC propellant in liquid form, but is not

soluble when combined with the HFC propellant in its crystalline form. The combination of prilocaine base in liquid form and HFC propellant forms a stable liquid solution having an oily consistency (see col. 3, lines 1-15).

Henry teaches that the association of liquid prilocaine base with HFC propellants has been found to allow its use as a solubilizing agent for dissolving and/or dispersing other medicaments within HFC propellants. In particular, prilocaine base can be used as a solubilizing aid for other local **anesthetics**, most of which are not ordinarily soluble in HFC propellants. For example, prilocaine base can be used in HFC propellants in combination with the anesthetics procaine, cocaine, chloroprocaine, tetracaine, mepivacaine, **lidocaine, bupivacaine**, etidiocaine, ropivacaine, and **benzocaine**. Prilocaine may be used in the preparation of HFC aerosol formulations that are used in topical delivery (e.g., skin wounds, hollow viscus and body cavity delivery), and may be used to solubilize, disperse and/or form stable suspensions with other medicaments including, for example, **anti-inflammatory drugs**, antibiotics, **steroids**, antiseptics and disinfectants, etc. Other prilocaine based aerosol formulations which may be used include analgesics, benzodiazepines and antibiotics including antivirals, **antifungals**, scabicides, antiprotozoals, etc (see paragraph bridging columns 5 and 6).

It would have been obvious to one of ordinary skill in the art at the time the invention was made given the general teachings of Beutler's disclosures on foamable emulsion formulations comprising a propellant, to have looked in the art for specific propellants and other suitable active agents, as taught by Henry, that can be delivered

via said base formulation with reasonable expectation of successfully preparing efficient foam formulations. In other words, Beutler teaches the foamable emulsions and discloses that propellants such as nitrous oxide can be employed. At the time of invention, it was known that HFA propellants are more suitable and more environmentally friendly. Also more commonly used in the field. Thus one of ordinary skill in the art would have been motivated to substitute the nitrous oxide of Beutler with a better propellant such as HFAs as taught by Henry. Furthermore one of ordinary skill in the art would have been motivated to implement other active agents in the foam base formulation of Beutler for easy and efficient delivery of various active agents to more patients in need of such treatments. Thus, the claims would have been obvious because the **substitution** of one known element for another would have **yielded predictable results** to one of ordinary skill in the art at the time of the invention.

Claims 4 and 10 are rejected under 35 U.S.C. 103(a) as being unpatentable over Beutler et al (4,808,388) in view of Henry (5,858,331) as applied to claim 1 above and in further view of Arkin et al (US 20050042182).

Beutler et al and Henry, discussed above lack disclosure on specific active agents. This deficiency is cured by Arkin et al.

Arkin et al teaches topical foamable compositions containing as an active agent, urea (see abstract). The said compositions may further comprise one or more active

ingredients, such as non-steroidal anti-inflammatory agents including ketoprofen and diclofenac; steroidal anti-inflammatory agents including dexamethasone, beclomathasone, halcinonide, flucioninde, etc. Also exemplary antibacterials including antibiotics and antifungals such as nystatin, tolnaftate, clotrimazole, etc (see [0135], [0136], [0139], [0140], [0143]).

It would have been obvious to one of ordinary skill in the art at the time the invention was made given the general teachings of the combined references of Beutler and Henry on foamable emulsion formulations comprising active agents and a propellant, to have looked in the art for other suitable active agents, as taught by Arkin et al with reasonable expectation of successfully preparing efficient foam formulations for delivery of various active agents to the desired site. In other words, Beutler and Henry teach foamable emulsions comprising HFA propellants and various active agents or classes of active agents. Arkin et al teach specific agents from each class of actives such as specific anti-inflammatory agents suitable for topical delivery. Thus one of ordinary skill in the art would have been motivated to implement other active agents in the foam base formulation of Beutler and Henry for easy and efficient delivery of various active agents to more patients in need of such treatments. In conclusion, **all the claimed elements** were known in the prior art and one skilled in the art could have combined the elements as claimed by known methods with no change in their respective functions, and the combination would have yielded predictable results to one of ordinary skill in the art at the time of the invention.

Claims 1 and 3-5 and 12-13 are rejected under 35 U.S.C. 103(a) as being unpatentable over Sachetto (WO 9603115) in view of Davis (5,143,717).

Sachetto teaches aqueous foamable compositions comprising **active agents** surfactants and foaming agents. The foaming agent is preferably a so-called liquefied gas, including butane, isobutene or environmentally friendly propellants such as **HFA 134a and HFA 227** (see page 4 and Table 1). Such foamable formulations have been exemplified in examples 1-21. Tables such as Table IV, discloses ingredients used in examples 10-14, which include a foaming agent.

Sachetto also discloses that the surfactant or mixture of surfactants incorporated in the compositions of the invention can be chosen from those which have an effective emulsifying action in relation to water and the foaming agent (see page 5). The formulations may comprise; a major amount by weight of water, a foaming agent, at least one foam-stabilizing and emulsifying surfactant, a water-soluble polymer, an effective amount of active substance and one or more pharmaceutical additive (see page 6). The active agents may include anti-inflammatory agents such as hydrocortisone, budesonide, beclomethasone dipropionate, etc (see page 8). While, it is expected for the formulations of Sachetto, comprising water and oily surfactants to be an emulsion, Sachetto does not specifically recite that limitation. However this is cured by Davis.

Davis discussed above, teaches emulsions where the oil phase can be a solid or semi-solid at room temperature.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to have combined the teachings of Sachetto and Davis on forming foam compositions with a reasonable expectation of successfully preparing stable foam formulations for treating various disorders topically. Sachetto teach an alcohol-free foam composition comprising water and surfactants and Davis teaches a foam formulation where the oil phase is solid at room temperature. Sachetto discloses that propellants such as HFAs are suitable and environmentally friendly propellants and for foam formulations. In other words, **all the claimed elements** were known in the prior art and one skilled in the art could have combined the elements as claimed by known methods with no change in their respective functions, and the combination would have yielded predictable results to one of ordinary skill in the art at the time of the invention.

Claims 1 and 3-13 are not allowable.

Response to Arguments

Applicant's arguments with respect to claims 1 and 3-13 have been considered but are moot in view of the new ground(s) of rejection.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Mina Haghighatian whose telephone number is (571)272-0615. The examiner can normally be reached on core office hours.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Johann Richter can be reached on 571-272-0646. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Mina Haghighatian/

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